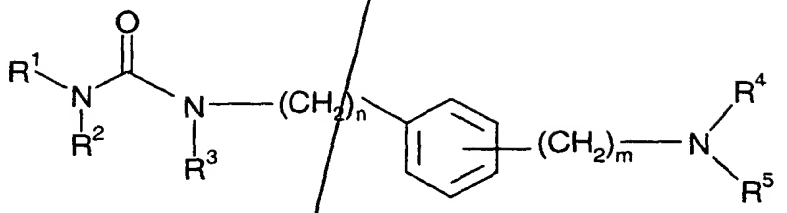
CLAIMS

1. A compound according to formula I



I

wherein

m and n is each and independently an integer of from 1-3, and one or more of the hydrogens in such an alkylene-chain may optionally be substituted by anyone of C_1 - C_6 alkyl, C_1 - C_6 alkoxy, or hydroxy; *or*

one or more of the methylene groups may optionally be substituted by a heteroatom such as O, N or S;

R^1 is selected from hydrogen, a branched or straight C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_8 cycloalkyl, C_4-C_8(alkyl-cycloalkyl) wherein the alkyl is C_1-C_2 alkyl and the cycloalkyl is C_3-C_6 cycloalkyl;

R^2 is selected from any of

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl;

(iii) -[$(CH_2)_q$- aryl];

(iv) -[$(CH_2)_r$- heteroaryl] where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;
and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below; and wherein q and r is each and independently an integer of from 0 to 3;

(v) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally susbtituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;
and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) C_6-C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

or

R^1 and R^2 may optionally form a heterocyclic ring;

R^3 is selected from anyone of

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(v) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) -[(C_3-C_6 cycloalkyl)-$(CH_2)_q$] wherein q is an integer of from 1 to 3;

R^4 is selected from

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl

may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(v) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally susbtituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;
and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi) C_6-C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

R^5 is selected from anyone of

(i) hydrogen;

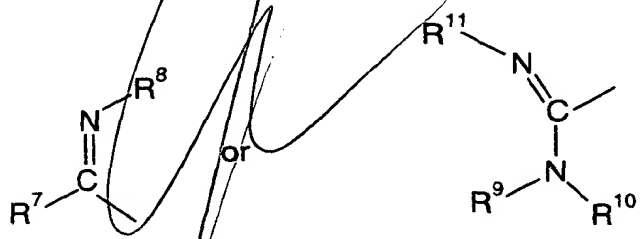
(ii) a straight or branched C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(v) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(vi)



;

wherein

R^7, R^8, R^9, R^{10} and R^{11} is each and independently selected from

(a) hydrogen;

(b) a straight or branched C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl;

(c) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

(d) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(e) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally susbtituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined below;

(f) C_6-C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined below;

or

R^4 and R^5 may optionally form a heterocyclic ring;

Y is each and independently selected from any of hydrogen, CH_3; —$(CH_2)_{p1}CF_3$; halogen; C_1-C_3 alkoxy; hydroxy; -NO_2; -OCF_3; —$CONR^aR^b$; —$COOR^a$; —COR^a; —$(CH_2)_{p2}NR^aR^b$; —$(CH_2)_{p3}CH_3$, $(CH_2)_{p4}SOR^aR^b$; —$(CH_2)_{p5}SO_2R^a$; —$(CH_2)_{p6}SO_2NR^a$; C_4-C_8(alkyl-cycloalkyl) wherein alkyl is C_1-C_2 alkyl and cycloalkyl is C_3-C_6 cycloalkyl; 1 or 2 heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O; and oxides such as N-oxides or sulfoxides; and wherein

R^a and R^b is each and independently selected from hydrogen, a branched or straight C_1-C_6 alkyl, C_1-C_6 alkenyl, C_3-C_8 cycloalkyl; and wherein

p^1, p^2, p^3, p^4, p^5 and p^6 is each and independently 0, 1 or 2;

as well as pharmaceutically acceptable salts, isomers, hydrates, isoforms and prodrugs thereof.

2. A compound according to formula I of claim 1, wherein

m=n=1

R^1 is selected from

(i) hydrogen;

(ii) a branched or straight C_1-C_6 alkyl; or

(iii) C_3-C_8 cycloalkyl;

R^2 is selected from any of

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl;

(iii) -[$(CH_2)_q$- aryl];

(iv) -[$(CH_2)_r$- heteroaryl] where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;
and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents **Y** where each **Y** is as defined in claim 1; and wherein q and r is each and independently an integer of from 0 to 3;

(v) C_3-C_6 cycloalkyl, optionally comprising one or more unsaturations and optionally susbtituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O;
and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(vi) C_6-C_{10} aryl, optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(vii) heteroaryl having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

or

R^1 and R^2 may optionally form a heterocyclic ring;

R^3 is selected from anyone of

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(vi) -[(C_3-C_6 cycloalkyl)-$(CH_2)_q$] wherein q is an integer of from 1 to 3;

R^4 is selected from

(i) hydrogen;

(ii) a straight or branched C_1-C_6 alkyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) C_6-C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

R^5 is selected from anyone of

(i) hydrogen;

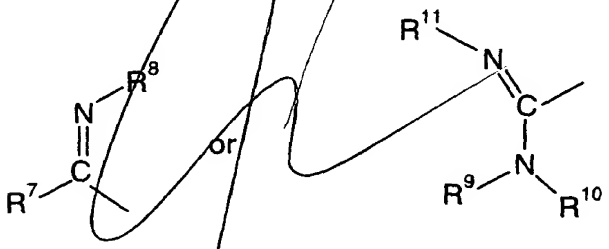
(ii) a straight or branched C_1-C_6 alkyl;

(iii) -[$(CH_2)_q$-aryl] wherein q is 0 or 1, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(iv) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(v) C_3-C_6 cycloalkyl, optionally comprising one or more unsaturations and optionally substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(vi)



;

wherein

R^7, R^8, R^9, R^{10} and R^{11} is each and independently selected from

(a) hydrogen;

(b) a straight or branched C_1-C_6 alkyl or C_2-C_6 alkenyl;

(c) -[$(CH_2)_q$-aryl] wherein q is an integer of from 0 to 3, and wherein the aryl may optionally be substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1;

(d) heteoaryl-(C_5 - C_{10} alkyl), where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O, and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(e) C_3-C_{10} cycloalkyl, optionally comprising one or more unsaturations and optionally susbtituted by one or more heteroaryl(s) where the heteroaryl has from 5 to 10 atoms and the heteroatom being selected from any of S, N and O; and wherein the aryl and heteroaryl may optionally and independently be substituted by 1 or 2 substituents Y where each Y is as defined in claim 1;

(f) C_6-C_{10} aryl, optionally and independently substituted by one or more heteroaryl(s) having from 5 to 10 atoms and the heteroatom(s) being selected from any of S, N and O and wherein the heteroaryl may optionally and independently be substituted by 1 or 2 substituents **Y** wherein each Y is as defined in claim 1;

or

R^4 and R^5 may form a heterocyclic ring which may optionally and independently be substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 1.

3. A compound according to claim 24, wherein

m=n=1

R^1 is selected from

(i) a straight or branched C_1-C_6 alkyl; or

(ii) C_3-C_8 cycloalkyl;

R^2 is selected from

(i) methyl; or

(ii) phenyl optionally substituted by 1 or 2 substituents Y wherein each Y is as defined in claim 23;

R^3 is selected from

(i) -CH_2-phenyl, optionally substituted by 1 or 2 subtituents Y where Y is as defined in claim 23;

(ii) -CH_2-cyclohexyl *or* -CH_2-cyclopentyl;

R^4 is selected from

(i) hydrogen; or

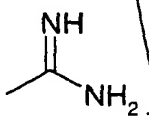
(ii) methyl;

R^5 is selected from

(i) hydrogen;

(ii) methyl;

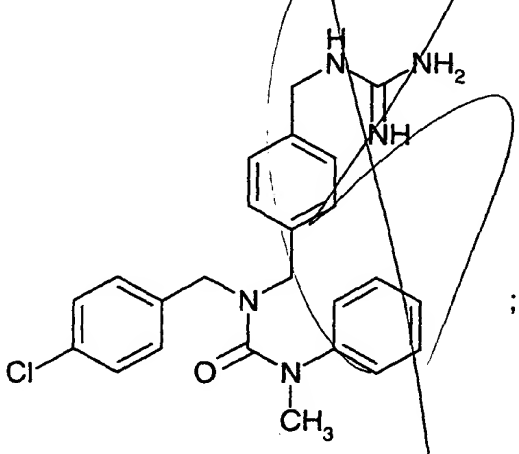
(iii)



;

R^4 and R^5 together form a heterocyclic ring, optionally substituted by 1 or 2 substituents Y, where Y is as defined in claim 1.

4. A compound selected from :



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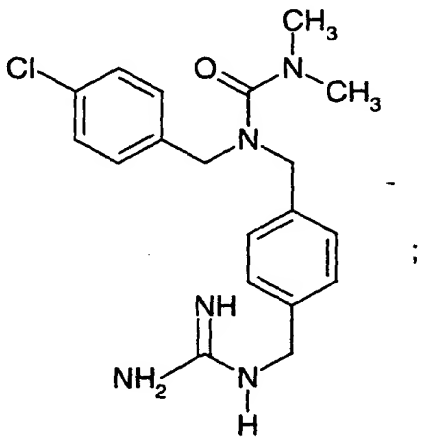

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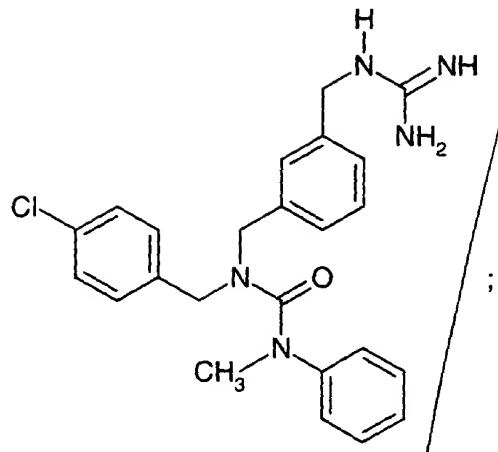

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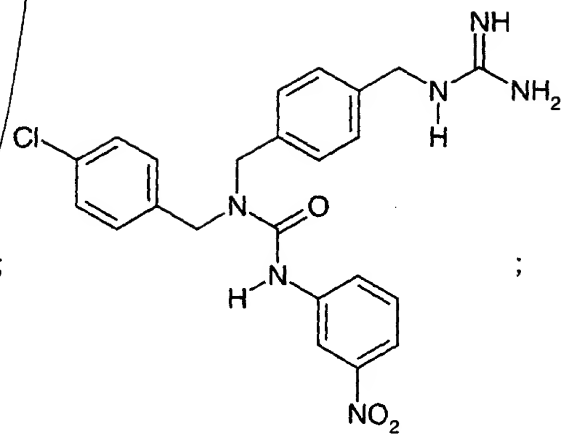

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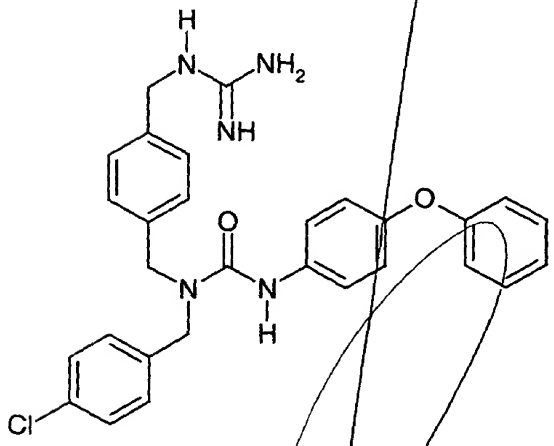

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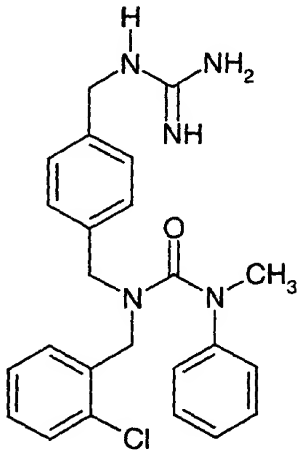

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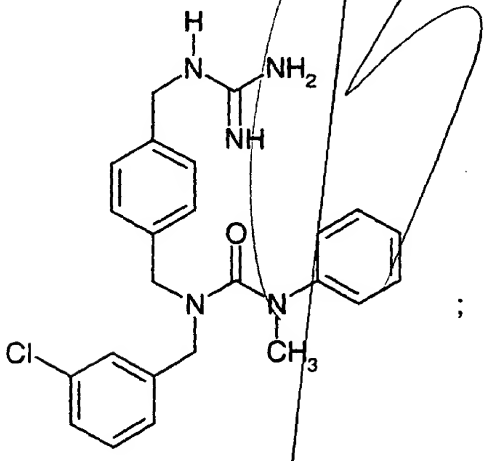

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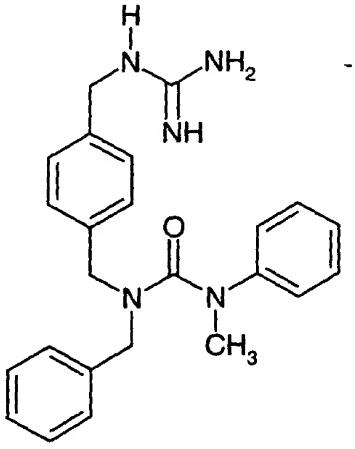

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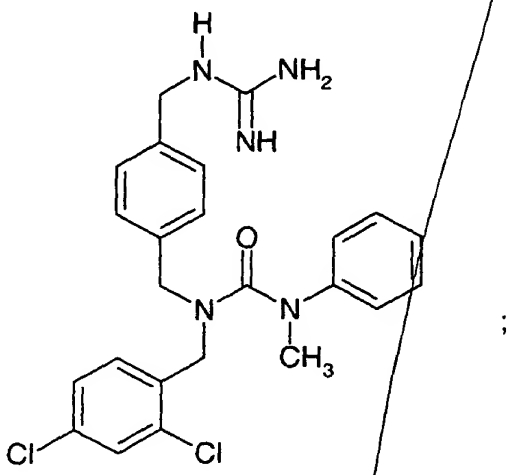

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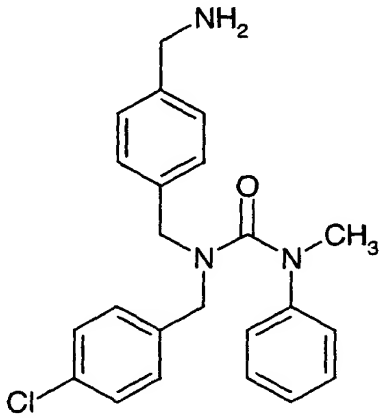

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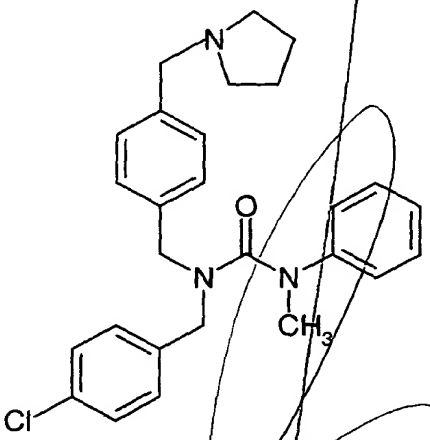

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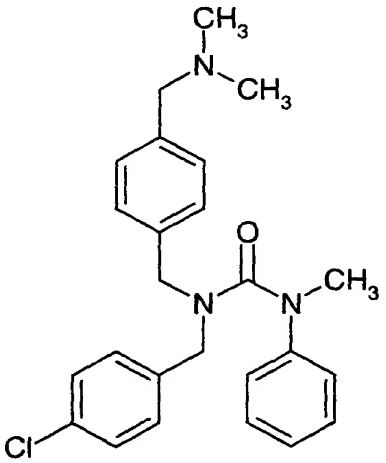

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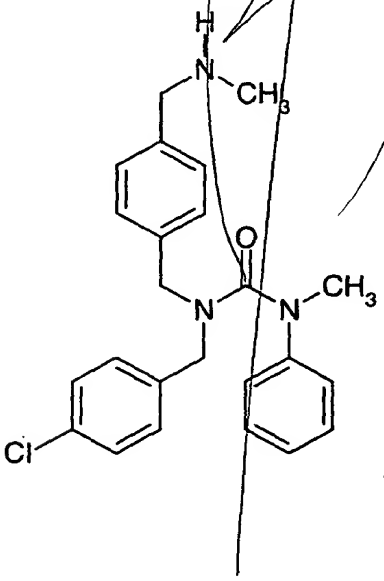


5. A compound according to any of the preceding claims, in form of its hydrochloride, sulfate, tartrate or citrate salts.

6. A compound according to any of claims 1-5 for use in therapy.

7. A compound according to claim 6, wherein the therapy is pain management.

8. A compound according to claim 6, wherein the therapy is directed towards gastrointestinal disorders.

9. A compound according to claim 6, wherein the therapy is directed towards spinal injuries.

10. A compound according to claim 6, wherein the therapy is directed to disorders of the sympathetic nervous system.

11. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of pain.

12. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of gastrointestinal disorders.

13. Use of a compound according to formula I of claim 1 for the manufacture of a medicament for use in the treatment of spinal injuries.

14. A compound according to any of claims 1-10, further characterised in that it is isotopically labelled.

15. Use of a compound according to claim 14 as a diagnostic agent.

16. An isotopically ~~labelled~~ labeled compound of ~~the~~ formula I of claim ~~1~~ 23.

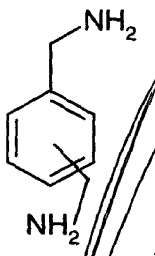
17. A diagnostic agent comprising a compound of the formula I of claim 1.

18. A pharmaceutical composition comprising a compound of ~~the~~ formula I according to claim ~~1~~ 23 as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.

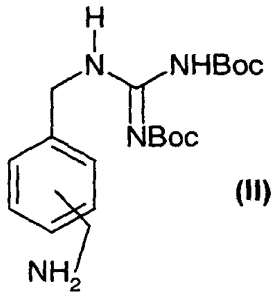
19. A process for the preparation of a compound of the formula I according to claim 1, whereby

A)

(i) bis-amino xylylene of the formula

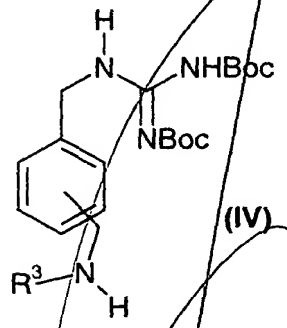


is converted into mono-(diBoc)-guanidinomethyl of the formula (II)



(II)

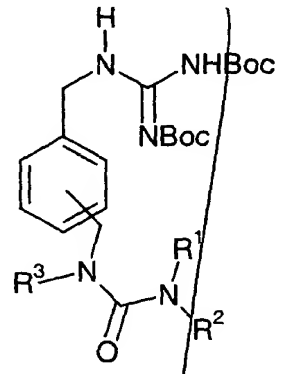
which thereafter is reacted with an aldehyde, providing a secondary amine of the general formula IV



(IV)

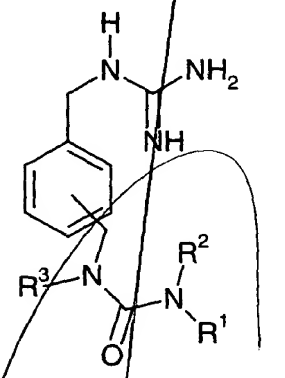
wherein R^3 is as defined in formula I of claim 1;

(ii) compound IV is subjected to an urea formation, providing a compound of the formula (VI)



(VI)

which finally is deprotected, providing a compound of the general formula VII



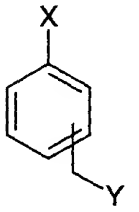
(VII)

wherein

R^1, R^2 and R^3 are as defined in formula I of claim 1; *or*

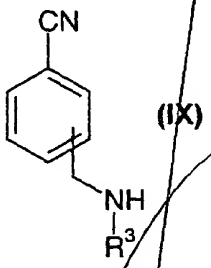
B)

(i) a compound of the formula (VIII)



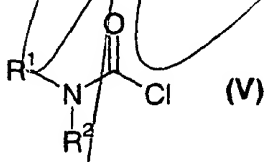
(VIII)

wherein X is CN and Y is CHO, is subjected to a reductive amination using a primary amine R^3NH_2 wherein R^3 is as as defined in formula I of claim 1, providing a compound of the formula (IX)



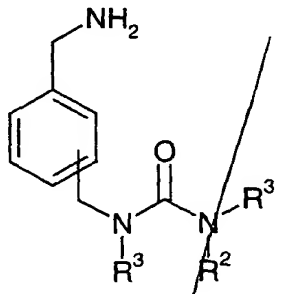
(IX)

wherein R^3 is as defined in formula I of claim 1, which thereafter is subjected to an urea reaction by using a chloroformate of the formula (V)



(V)

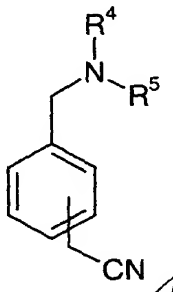
which finally is reduced, providing a compound of the formula (XI)



(XI)

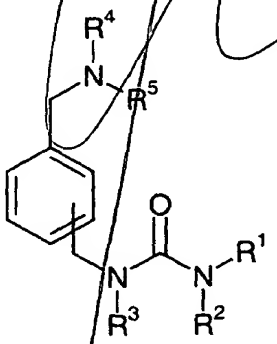
; *or*

(ii) compound (VIII) wherein X is CH_2Br and Y is CN, is reacted with an amine R^4R^5NH wherein R^4 and R^5 are as defined in formula I of claim 1, providing a compound of the formula (XII)



(XII)

which is reduced and reacted with an aldehyde R^3CHO wherein R3 is as defined in formula I of claim 1, and finally subjected to an urea action with a chloroformate (V) as in step (i), providing a compound of the formula (XV)



(XV)

wherein R^1, R^2, R^3, R^4 and R^5 are as defined in formula I of claim 1.

20. A method for the treatment of pain, whereby an effective amount of a compound of the formula I according to claim 1 is administered to a subject in need of pain management.

21. A method for the treatment of gastrointestinal disorders, whereby an effective amount of a compound of the formula I according to claim 1, is administered to a subject suffering from said gastrointestinal disorder.

22. A method for the treatment of spinal injuries, whereby an effective amount of a compound of the formula I according to claim 1, is administered to a subject suffering from said spinal injury.